

CLAIMS

1. A purified nucleic acid fragment, characterized  
5 in that it comprises all or part of a sequence encoding  
a human endogenous retroviral sequence, which has at  
least env-type retroviral motifs, corresponding to the  
sequence SEQ ID NO: 1 or to a sequence exhibiting a  
level of homology with the said sequence SEQ ID NO: 1  
10 greater than or equal to 80% on more than 190  
nucleotides or greater than or equal to 70% on more  
than 600 nucleotides for the env-type domains.

2. The nucleic acid fragment as claimed in  
claim 1, characterized in that it has retroviral motifs  
15 corresponding to an env domain and corresponding to the  
sequence SEQ ID NO: 1 and retroviral motifs  
corresponding to a gag domain and corresponding to the  
sequence SEQ ID NO: 2 or to a sequence exhibiting a  
level of homology greater than or equal to 80% on more  
20 than 190 nucleotides or greater than or equal to 70% on  
more than 600 nucleotides for the env-type domains and  
a level of homology greater than or equal to 90% on  
more than 700 nucleotides or greater than or equal to  
70% on more than 1 200 nucleotides for the gag-type  
25 domains, the said motifs having no insertion or  
deletion of more than 200 nucleotides.

3. A nucleic acid fragment, characterized in that  
it comprises a segment of a sequence as claimed in  
claim 1 or claim 2 and in particular the sequence  
30 SEQ ID NO: 3-22, 28 and 61, the complementary nucleic  
sequences and the reverse sequences complementary to  
the preceding sequences as well as fragments derived  
from the coding regions of the preceding sequences  
corresponding to a shifting frame greater than or equal  
35 to 14 nucleotides or their complementary sequences.

4. Transcripts, characterized in that they are  
generated from the sequences as claimed in any one of  
claims 1 to 3.

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5. A diagnostic reagent for the differential detection of complete or partial human endogenous nucleic sequences, having retroviral motifs, selected from the sequences SEQ ID NO: 1 and/or SEQ ID NO: 2, characterized in that it is selected from the group consisting of the sequences SEQ ID NO: 1-22, 28, 37-57, 59-61 and 121-122, the complementary nucleic sequences and the reverse sequences complementary to the preceding sequences, of nucleotide fragments capable of defining or of identifying the sequences SEQ ID NO: 1 and/or SEQ ID NO: 2 and any flanking sequence or any sequence overlapping them as well as of fragments derived from the coding regions of the sequences SEQ ID NO: 1-22 and 61, corresponding to a shifting frame greater than or equal to 14 nucleotides or their complementary sequences, optionally labeled with an appropriate label.

6. The reagent as claimed in claim 5, characterized in that it is chosen from the regions situated between nucleotides 3065 and 4390, nucleotides 6965 and 9550 or nucleotides 2502-2865 of SEQ ID NO: 3.

7. The reagent as claimed in claim 5, characterized in that it is selected from the sequences SEQ ID NO: 37-57, 59-60 and 121-122 and in that it is capable of being used as a primer.

8. The reagent as claimed in claim 5, characterized in that it is selected from the following sequences:

- a fragment of 1505 nt amplified by the pair of primers SEQ ID NO: 37 and SEQ ID NO: 38 (primers G1F and G1R),

- a fragment of 2529 nt amplified by the pair of primers SEQ ID NO: 45 and SEQ ID NO: 46 (primers E1F and E1R),

- a fragment of 182 nucleotides, repeated twice, situated upstream of the gag domain at positions 2502-2611/2613-2865,

and in that it is capable of being used as a probe.

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9. The reagent as claimed in claim 5, characterized in that it is chosen from the group consisting of the fragments encoding or not encoding all or part of enverin, in particular the fragments comprising at least 14 nucleotides and more particularly the fragments encoding the C-terminal portion of enverin, either from the amino acid 291, or from the amino acid 321, starting from the codon encoding the first methionine.

10. A method for the rapid and differential detection of the endogenous retroviral nucleic sequences of the env or env and gag type, their normal or pathological variants, by hybridization and/or gene amplification, carried out using a biological sample, which method is characterized in that it comprises:

(a) a step in which a biological sample to be analyzed is brought into contact with at least one probe as claimed in claim 5, claim 6 or claim 8, and

(b) a step in which the product(s) resulting from the nucleotide sequence-probe interaction is detected by any appropriate means.

11. The method of detection as claimed in claim 10, characterized in that it comprises:

\* prior to step (a):

. a step of preparing the relevant biological tissue or fluid,

. a step of extracting the nucleic acid to be detected, and

. at least one gene amplification cycle carried out with the aid of at least one reagent as claimed in any one of claims 5 to 7, and

\* subsequent to step (b):

. a step of comparing the nucleic sequences obtained in the said biological sample with the human endogenous retroviral sequences as claimed in any one of claims 1 to 3, by any appropriate means and in particular by sequencing, Southern blotting, restriction cleavage, SSCP or any other method which makes it possible to identify an insertion or a

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C1

Sub  
B3

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deletion or a single mutation between the various sequences compared.

12. A method of detecting the transcripts as claimed in claim 4, characterized in that it comprises:

5 - collecting messenger RNAs obtained from control biological samples and from a similar sample collected from patients, and

- the qualitative and/or quantitative analysis of the said mRNAs by *in situ* hybridization, by dot-blot, Northern blotting, RNase mapping or RT-PCR, with the aid of a diagnostic reagent as claimed in any one of claims 5 to 9.

13. Chimeric sequences, characterized in that they consist of a fragment of 17 to 40 nucleotides of a flanking sequence selected from the group consisting of transcripts and cDNAs of the genomic sequences, which encode all or part of a factor, whose function, regulation/deregulation or alteration is associated with the normal or pathological expression or with the regulation/deregulation of motifs belonging to said  
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20  
25  
HERV-7q family, these sequences corresponding to nucleotide sequences encoding genes situated in flanking regions situated upstream and/or downstream of a retroviral sequence of the said HERV-7q family and in which one of the ends cannot be at a distance exceeding 120 kb, associated with an endogenous retroviral motif of the HERV-7q type comprising between 17 and 40 nucleotides as claimed in claims 1 to 4.

14. A method for the detection and/or evaluation of an overexpression/underexpression or of a modification of at least one of the endogenous retroviral sequences or fragments of sequences of the HERV-7q type and/or of their associated flanking sequences, as claimed in any one of claims 1 to 9, characterized in that it  
30  
35 comprises:

- depositing on an appropriate support, cDNA obtained from clones, PCR products obtained from genomic DNA, RT-PCR products obtained from transcripts or from specific oligonucleotide sequences, the said

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5 DNA sequences being endogenous retroviral sequences or  
fragments of sequences of the HERV-7q type and/or their  
flanking sequences, consisting of transcripts and cDNAs  
of the genomic sequences, which encode all or part of a  
factor, whose function, regulation/deregulation or  
alteration is associated with the normal or  
pathological expression or with the regulation/  
deregulation of motifs belonging to the said HERV-7q  
family, these sequences corresponding to nucleotide  
10 sequences encoding genes situated in flanking regions  
situated upstream and/or downstream of a retroviral  
sequence of the said HERV-7q family and in which one of  
the ends cannot be at a distance exceeding 120 kb,  
and/or a chimeric sequence as claimed in claim 13,

15 - the hybridization of the said support with at  
least one appropriately labeled probe obtained, for  
example, by retrotransposition of an RNA mixture  
obtained from biological cells, tissues or fluids  
obtained from controls reputed to be normal, from  
20 members of various ethnic populations, from patients  
suffering from pathological conditions often associated  
with expression of retroviruses, such as tumor  
processes, or such as autoimmune diseases, and

- the detection of the hybrids formed.

25 15. The method as claimed in claim 14,  
characterized in that the said transcript or cDNA is  
selected from the group consisting of the sequences SEQ  
ID NO: 62-67 and 119 and their fragments corresponding  
to a shifting frame greater than or equal to 14  
30 nucleotides or their complementary sequences.

16. The method as claimed in claim 14 or claim 15,  
characterized in that the said support comprises, in  
addition, any endogenous or exogenous retroviral  
sequence.

35 17. The kit for the detection and/or evaluation of an  
autoimmune disease and in particular of  
neuropathological conditions with an autoimmune  
etiology, characterized in that it comprises, in

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addition to the buffers necessary for carrying out a method according to any one of claims 14 to 16:

- diagnostic reagents A as claimed in any one of claims 5 to 9, and

5       - reagents B consisting of the transcripts and cDNAs of the genomic sequences, which encode all or part of a factor, whose function, regulation/de-regulation or alteration is associated with the normal or pathological expression or with the regulation/de-regulation of motifs belonging to said HERV-7q family, these sequences corresponding to nucleotide sequences encoding genes situated in flanking regions situated upstream and/or downstream of a retroviral sequence of said HERV-7q family, of which one of the ends cannot be  
10       at a distance exceeding 120 kb,

15       - which reagents are preferably attached to an appropriate support.

18. The kit as claimed in claim 17, characterized in that said reagents B are selected from the group  
20       consisting of the sequences SEQ ID NO: 62-67 and 119 and their fragments corresponding to a shifting frame greater than or equal to 14 nucleotides or their complementary sequences.

19. Translational products, characterized in that they  
25       are encoded by a nucleotide sequence as claimed in any one of claims 1 to 4.

20. A peptide, characterized in that it is capable of being expressed with the aid of a nucleotide sequence selected from the group consisting of the sequences  
30       SEQ ID NO: 1-22, 28 and 61 as claimed in any one of claims 1 to 4.

21. The peptide as claimed in claim 20, characterized in that it includes the derived peptides comprising between 5 and 540 amino acids and in particular a  
35       fragment of 538 amino acids, starting at the first methionine of the sequence SEQ ID NO: 26 (enverin).

22. The peptide as claimed in claim 20 or claim 21, characterized in that it is selected from the group consisting of:

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the sequences SEQ ID NO: 23-36;  
the sequence SEQ ID NO: 58;  
a C-terminal fragment of the sequence  
SEQ ID NO: 26, either from the amino acid 291, or from  
5 the amino acid 321, starting from the first methionine  
of the sequence SEQ ID NO: 26;

a peptide of the CKS-17/CKS-25 type present  
in one of the sequences SEQ ID NO: 23-36 or 58; and

the peptides having affinity with one of the  
10 haplotypes of the class I or class II HLA system and in  
particular the fragments 399-471, 244-271 of enverin,  
as well as the peptides having the sequence  
SEQ ID NO: 68-118, in accordance with Table I.

23. The peptide as claimed in any one of claims 20 to  
15 22, characterized in that it is obtained from nucleic  
sequences as claimed in any one of claims 1 to 4, in  
which at least one non-sense codon may be replaced with  
a codon encoding one of the following amino acids: Phe  
(F), Leu (L), Ser (S), Tyr (Y), Cys (C), Trp (W), Gln  
20 (Q), Arg (R), Lys (K), Glu (E) or Gly (G).

24. Immunogenic or vaccine compositions for protecting  
against autoimmune diseases, in particular in at motif  
selected risk subjects, characterized in that it  
comprises at least one peptide comprising at least one  
25 motif of the CKS type and/or at least one motif  
selected from the group consisting of the peptides  
having affinity with one of the haplotypes of the class  
I or class II HLA system and at least one  
pharmaceutically acceptable vehicle.

25. The composition as claimed in claim 24,  
30 characterized in that said peptide having affinity with  
one of the haplotypes of the class I or class II HLA  
system is selected from the group consisting of the  
peptides as defined in Table I.

26. The composition as claimed in claim 24 or claim  
35 25, characterized in that said peptide has the sequence  
SEQ ID NO: 120.

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27. An antibody, characterized in that it is directed against one or more of the peptides as claimed in any one of claims 20 to 23.

28. A pharmaceutical composition, characterized in that it comprises neutralizing antibodies produced from the peptides of Table I (SEQ ID NO: 68-118) and their homologues.

29. A method for the differential immunological screening of normal or pathological human endogenous retroviral sequences of the HERV-7q family, characterized in that it comprises bringing a biological sample into contact with an antibody as claimed in claim 27, the reading of the result being visualized by an appropriate means, in particular EIA, ELISA, RIA, fluorescence.

30. A method for the identification and detection of endogenous retroviral motifs which are abnormally expressed in the context of pathological conditions associated with cancer, or of neuropathological conditions, in particular autoimmune neuropathological conditions, at the forefront of which is multiple sclerosis, characterized in that it comprises the comparative analysis of the sequences extracted from a biological sample and the sequences as claimed in any one of claims 19 to 23.

31. An application of the sequences as claimed in any one of claims 1 to 9, 13, 14 or 19 to 23 to the diagnosis of, to the prognosis of, to the evaluation of genetic susceptibility to, any induced, congenital or acquired human diseases, in particular those with cancerous, autoimmune and/or neurological components, such as multiple sclerosis, the associated syndromes and the neurodegenerative diseases in which all or part of the sequences as claimed in to any one of claims 1 to 5 and related endogenous or exogenous forms are involved.

32. Hybrid nucleic sequences, characterized in that they comprise sequences or motifs as claimed in any one of claims 1 to 9, combined with sequences or motifs of

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endogenous origin or of exogenous origin or induced exogenously.

33. A recombinant cloning or expression vector, characterized in that it comprises a nucleic sequence as claimed in any one of claims 1 to 4.

34. An immunogenic or vaccine composition, characterized in that it comprises a vector including at least one nucleic sequence encoding a peptide as defined in Table I, optionally combined with a sequence encoding a motif of the CKS-17 type.

35. A gene therapy vector, characterized in that it comprises all or part of the endogenous retroviral nucleic sequences of the HERV-7q type as claimed in any one of claims 1 to 4.

36. The vector as claimed in claim 35, characterized in that said sequences are selected from the group consisting of the sequences SEQ ID NO: 2, 20 and 21.

37. Transgenic animals, characterized in that they comprise all or part of a sequence of the HERV-7q type (SEQ ID NO: 1-22, 28 and 61).

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